



US006001395A

United States Patent [19]

Coombes et al.

[11] Patent Number: **6,001,395**
[45] Date of Patent: **Dec. 14, 1999**

[54] **POLYMERIC LAMELLAR SUBSTRATE PARTICLES FOR DRUG DELIVERY**

[75] Inventors: **Allan Gerald Arthur Coombes; Stanley Stewart Davis**, both of Nottingham; **Diane Lisa Major**, London; **John Michael Wood**, Hertsfordshire, all of United Kingdom

[73] Assignee: **Danbiosyst UK Limited**, Nottingham, United Kingdom

[21] Appl. No.: **08/983,156**

[22] PCT Filed: **Jul. 15, 1996**

[86] PCT No.: **PCT/GB96/01695**

§ 371 Date: **Mar. 30, 1998**

§ 102(e) Date: **Mar. 30, 1998**

[87] PCT Pub. No.: **WO97/02810**

PCT Pub. Date: **Jan. 30, 1997**

[30] **Foreign Application Priority Data**

Jul. 13, 1995 [GB] United Kingdom 9514285

[51] Int. Cl.⁶ **A61K 9/16; A61K 47/34**

[52] U.S. Cl. **424/501; 424/426; 424/490**

[58] Field of Search 424/486, 426, 424/458, 428, 459, 490, 501; 514/952; 428/402, 402.24; 427/2.14

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,492,720 1/1985 Mosier .
5,827,531 10/1998 Morrison et al. .
5,869,103 2/1999 Yeh et al. .

FOREIGN PATENT DOCUMENTS

WO 95/11010
A1 4/1995 WIPO .
WO 95/35097
A1 12/1995 WIPO .

OTHER PUBLICATIONS

Alpar, et al., "Identification of Some of the Physico-Chemical Characteristics of Microspheres which Influence the Induction of the Immune Response Following Mucosal Delivery," *Eur. J. Pharm. Biopharm.* 40(4):198-202 (1994).
Cohen, et al., "The pharmacokinetics of, and humoral responses to, antigen delivered by microencapsulated liposomes," *Proc. Natl. Acad. Sci. USA* 88:10440-44 (1991).
Eldridge, et al., "Biodegradable Microspheres as a Vaccine Delivery System," *Mol. Immunol.* 28(3):287-94 (1991).
Esparza, et al., "Parameters affecting the immunogenicity of microencapsulated tetanus toxoid," *Vaccine* 10(10):714-20 (1992).
Gray, et al., "B-cell memory is short lived in the absence of antigen," *Nature* 336:70-73 (1988).
Kalb, et al., "General crystallization behavior of poly(L-lactic acid)," *Polymer* 21(6):607-12; ACS Abstract No. 93:240075 (1980).
Khan, et al., "Immunopotential and Delivery Systems for Antigens for Single-Step Immunization: Recent Trends and Progress," *Pharm. Res.* 11(1):2-11 (1994).
Kreuter, et al., "Influence of hydrophobicity on the adjuvant effect of particulate polymeric adjuvants," *Vaccine* 6(3):253-56 (1988).
O'Hagan, et al., "Biodegradable microparticles as controlled release antigen delivery systems," *Immunology* 73(2):239-42 (1991); ACS Abstract No. 115:56995 (1991).

(List continued on next page.)

Primary Examiner—Edward J. Webman

Attorney, Agent, or Firm—Arnall Golden & Gregory, LLP

[57] **ABSTRACT**

The invention provides a composition for delivery of an active agent comprising a plurality of lamellar particles of a biodegradable polymer which is at least in part crystalline, and an active agent adsorbed to at least most of the particles. Preferably the biodegradable polymer is at least 5% by weight crystalline. Preferred biodegradable polymers are poly(L-lactide) (L-PLA) or copolymers or blends of L-PLA. The particles are especially useful for the immobilization of antigens or allergens for vaccines.

18 Claims, 4 Drawing Sheets

